

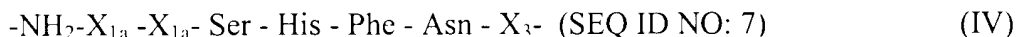
**IN THE SPECIFICATION:**

Please enter the following replacement paragraphs at page 20, line 12 to page 22, line 2:

--In one embodiment the TGF- $\alpha$  polypeptide, related polypeptide, mimetic or functional fragment is a TGF- $\alpha$  polypeptide as set forth in SEQ ID NO:1, SEQ ID NO:3, or a TGF $\alpha$  mimetic selected from the group consisting of formula I, formula II, formula III, formula IV, or formula V, wherein formula I is:



wherein  $R_1$  is  $-NH_2$ , or  $R_1$  is  $R_3-X_3$ , wherein  $R_3$  is a polyethylene glycol (PEG) attached to the free  $NH_2$  moiety of  $X_3$  (wherein  $X_3$  is Lys or Asp) and having a molecular weight of PEG of from about 2000 daltons to about 10,000 daltons, or one or more of the following seven amino acids from formula IV, including either L (natural) or D chiral orientations:



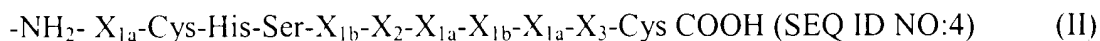
wherein  $X_{1a}$  is independently Val, Gly or Ala and  $X_3$  is Lys or Asp;

wherein T is the native sequence of human TGF $\alpha$  (SEQ ID NO. 1) from amino acid residue no. 8 (Cys) to amino acid residue no. 43 (Cys) consisting of native L amino acids; and wherein  $R_2$  is  $-COOH$  or one of more of the following seven amino acids, including either L (natural) or D chiral orientations, from formula V:



wherein  $X_4$  is Glu or Asp, wherein  $X_5$  is Leu or Ile, wherein  $X_6$  is Asp or Glu, and wherein  $X_{1c}$  is independently Val, Gly, or Ala.

The invention provides a peptide having TGF- $\alpha$  biological activity, comprising at least an 11-membered peptide compound of formula II:



wherein  $X_{1a}$ , and  $X_{1b}$  are independently Val, Gly, or Ala, wherein  $X_2$  is Tyr or Phe, wherein  $X_3$  is Arg or Lys, and wherein the two Cys moieties form a disulfide bond to create an 11-amino-acid functional peptide having a 10 member loop structure. In addition, at least one or more of the following amino acids of formula III may be added to the C terminus Cys moiety of formula II:

- X<sub>4</sub> - His - X<sub>1c</sub> - X<sub>4</sub> - X<sub>5</sub> - X<sub>6</sub> - X<sub>1c</sub> (SEQ ID NO: 5) (III)

wherein X<sub>4</sub> is Glu or Asp, wherein X<sub>5</sub> is Leu or Ile, wherein X<sub>6</sub> is Asp or Glu and wherein X<sub>1c</sub> is Val, Gly or Ala. Preferably, X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly and X<sub>1c</sub> is Ala thereby producing an 11, 12, 13, 14, 15, 16, 17 or 18 amino acid peptide. Preferably, X<sub>2</sub> is Tyr, and X<sub>3</sub> is Arg. Accordingly, in one embodiment the functional peptide of the invention has a sequence:

NH<sub>2</sub>-X<sub>1a</sub>-Cys-His-Ser-X<sub>1b</sub>-X<sub>2</sub>-X<sub>1a</sub>-X<sub>1b</sub>-X<sub>1a</sub>-X<sub>3</sub>-Cys-X<sub>4</sub>-His-X<sub>1c</sub>-X<sub>4</sub>-X<sub>5</sub>-X<sub>6</sub>-X<sub>1c</sub>-COOH (SEQ ID NO:6)

SEQ ID NO: 6 forms a 10 member loop structure with a 7 member tail that can be varied in length. In addition, SEQ ID NO: 6 can form dimmers comprising, for example, a 34-mer peptide. Accordingly, the functional peptide can be from about 10 to 18 amino acids in length (*e.g.* 10, 11, 12, 13, 14, 15, 16, 17, or 18 amino acids) wherein X<sub>1a</sub> is Val, X<sub>1b</sub> is Gly, X<sub>1c</sub> is Ala and X<sub>4</sub> is Glu and may also comprise hetero- or homo-dimers of various TGF- $\alpha$  peptides described herein. Such dimmers may have greater or reduced activities as compared to monomers.

The invention further provides an active TGF- $\alpha$ 57 polypeptide (SEQ ID NO:3), wherein TGF- $\alpha$ 57 is a 57 amino acid polypeptide having the formula VI:

Ser - Leu - Ser - Leu - Pro - Ala - Met - Human TGF $\alpha$  (SEQ ID NO: 3) (VI)

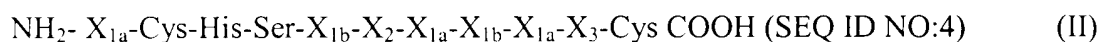
Wherein human TGF $\alpha$  is a 50 amino acid polypeptide having a sequence as set forth in SEQ ID NO:1.--

Please enter the following replacement paragraphs at page 52, lines 1-27:

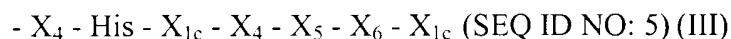
--The invention further provides a bifunctional compound that acts as a TGF $\alpha$  mimetic, comprising a compound of formula III:

Loop peptide N-terminus-linker-cyclic C<sub>4</sub>H<sub>8</sub>N<sub>2</sub>- linker- Loop peptide N-terminus (VII)

Wherein the linker moiety is designed to link the N-terminus of the Loop peptide to a nitrogen atom of the ring  $C_4H_8N_2$  and wherein the "loop peptide" comprises at least an 11-membered peptide compound of formula II:



wherein  $X_{1a}$  and  $X_{1b}$  are independently Val, Gly, or Ala;  $X_2$  is Tyr or Phe;  $X_3$  is Arg or Lys; and the two Cys moieties are linked via a disulfide bond to form an at least 11-amino acid functional peptide having TGF- $\alpha$  activity. Preferably, at least one or more of the following amino acids are added to the C terminus Cys moiety from formula III, below:



wherein  $X_4$  is Glu or Asp, wherein  $X_5$  is Leu or Ile, wherein  $X_6$  is Asp or Glu and wherein  $X_{1c}$  is Val, Gly or Ala. Preferably,  $X_{1a}$  is Val,  $X_{1b}$  is Gly and  $X_{1c}$  is Ala. Preferably the linker group is independently selected from the group consisting of substituted or unsubstituted  $C_{1-6}$  alkoxy, xylenyl, wherein the substitutions are selected from the group consisting of: oxo, epoxy, hydroxyl, chloryl, bromyl, fluoryl, and amino. Preferably,  $X_2$  is Tyr, and  $X_3$  is Arg. Most preferably, the functional peptide is 18 amino acids in length wherein  $X_{1a}$  is Val,  $X_{1b}$  is Gly,  $X_{1c}$  is Ala and  $X_4$  is Glu.--